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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

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09/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/618,577	BOSSY ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,17 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/2/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim 1 has been amended. Claims 1-12, 17 and 18 are pending and under consideration.

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is re-acknowledged. The instant amended claims are now commensurate with the 60/144,529 application filed July 19, 1999.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1-3, 5, 6, 9-12, 17 and 18 under 35 U.S.C. 102(e) as being anticipated by Ts'o et al (U.S. 5,962,237) is maintained for reasons of record.

Claim 1 is drawn to a method for identifying a proliferative disorder comprising contacting a sample of cells with a binding agent specific for a cell specific marker associated with a proliferative disorder and expressed by at least some of the cells, wherein the binding agent is bound to a magnetic beads and wherein the binding agent binds to cells expressing said marker; separating cells bound by the binding agent thereby obtaining a subpopulation of cells enriched for said cell specific marker; placing the enriched sample obtained thereby on a microscope slide; automatically screening the microscope slide at a plurality of coordinate using a microscope' automatically obtaining a plurality of images at locations on the microscope slide to which the enriched sample is bound and processing the plurality of images to identify the proliferative disorder. Claim 2 embodies the method of claim 1 wherein the binding agent is an antibody. claim 3 embodies the method of claim 1 wherein the sub-population is enriched for carcinoma cells. Claim 5 embodies the method of claim 1 wherein the separating is done by

negative selection. Claim 6 embodies the method of claim 2 wherein the antibody is monoclonal or polyclonal. Claim 9 embodies the method of claim 3 herein the carcinoma cells are from peripheral blood. Claim 11 embodies the method of claims 11 wherein the proliferative disorder is detected by immunohistochemistry. Claims 12 embodies the method of claim 1 wherein the proliferative disorder is detected by in situ hybridization. Claim 17 embodies the method of claim 1 wherein the cell specific marker is detected by immunohistochemistry, in situ hybridization, staining or a combination thereof. Claim 18 embodies the method of claim 1 wherein the image is a digital image.

Ts'o et al disclose a method of detecting cancer cell in peripheral blood comprising contacting a blood sample with primary antibodies which bind to hematopoietic cells followed by a second antibody that is conjugated to a magnetic bead in order to provide a fluid enriched for non-hematopoietic cells (column 3, lines 30-42, column 1, lines 24- 27 and lines 43-45) . Ts'o et al disclose that the antibodies are preferably monoclonal (column 10, lines 31-34). Ts'o et al disclose the placement of the enriched sample on a microscope slide (column 13, lines 12-25) and identification of circulating prostate cancer cells by immunohistochemistry and in situ hybridization (column 23, lines 24-27). Ts'o disclose the placement of the enriched sample on a microscope slide and identifying and acquiring a digital image of the cells on the slide by the use of a microscope was carried out automatically (column 17, lines 10-23). The imaging of the cells on the microscope slide fulfill the specific embodiment of claim 10 because acquiring a digital image simultaneously provides for both the acquisition of an image and the identification of a coordinate where a cell is located.

Applicant argues that the binding agents of Ts'o et al are bound via a secondary antibody to the magnetic bead and therefore fail the limitation of "separating cells bound by the binding agent from the source" since the binding antibody is not directly attached to the bead. This has been considered but not found persuasive. When given the broadest reasonable interpretation, the term "binding agent" encompasses the entirety of the magnetic bead and the attachment to the binding antibody.

Applicant argues that Ts'o et al fail to disclose "processing the plurality of images to identify the proliferative disorder". This has been considered but not found persuasive. The

limitation of processing the plurality of images to identify the proliferative disorder is a abstract step rather than a active method step, therefore it is not given patentable weight when distinguishing the prior art from the instant invention. However, Ts'o et al do disclose an automated method for acquiring a digital image of the cells on the slide by the use of a microscope.

The rejection of claims 1-4, 6-12, 17 and 18 under 35 U.S.C. 102(e) as being anticipated by Terstappen et al (U.S. 6,365,362) is maintained for reasons of record.

Claim 4 embodies the method of claim 1 wherein the separating is done by positive selection. Claim 7 embodies the method of claim 2 wherein the antibody recognizes an epithelial marker. Claim 8 embodies the method of claim 2 wherein the antibody is selected to avoid cross-reactivity with the beads.

Terstappen et al disclose a method of immunomagnetic enrichment of circulating cancer cells in peripheral blood (column 23, line 38, column 28, line 1) and immunohistochemical analysis (column 8, lines 54-56) of said enriched sample on a microscope slide (Figure 4, column 26, lines 1-4, column 18, lines 1-3), wherein the immunomagnetic particle is conjugated to an antibody which binds determinants found on non-hematopoietic cells. Terstappen et al disclose placing the enriched sample on a microscope slide (column 18, line 3, and the automated reading of the slide (column 18, lines 4-5). Terstappen et al disclose imaging with a digital camera which includes a 100X objective lens to detect cells stained with Wright Giemsa (column 12, lines6-8) or other microscope (column 8, lines 47-49) was used to read the enriched samples. Terstappen disclose antibodies which specifically bind to epithelial cell markers (column 11, lines 37-39). Terstappen et al disclose the selection of antibodies with minimal cross-reactivity (column 19, line 54 to column 22, line 11) and antibodies which are monoclonal (column 8, lines 30-36). The imaging of the cells on the microscope slide fulfill the specific embodiment of claim 10 because acquiring a digital image simultaneously provides for both the acquisition of an image and the identification of a coordinate where a cell is located.

Applicant argues that the limitations of "automatically scanning the microscope slide at a plurality of coordinates using a microscope; automatically obtaining a plurality of images at

location on the microscope slide, and processing the plurality of images to identify the proliferative disorder" are not disclosed by Terstappen et al. This has been considered but not found persuasive. Terstappen et al disclose imaging with a digital camera which includes a 100X objective lens to detect cells in the enriched sample on the microscope slide (column 12, lines6-8, column 8, lines 47-49) in order to "read" the enriched samples. The imaging of the cells on the microscope slide fulfill the specific embodiment of claim 10 because acquiring a digital image simultaneously provides for both the acquisition of an image and the identification of a coordinate where a cell is located, and thus fulfills the embodiments of scanning the microscope slide at a plurality of coordinates and obtaining a plurality of images at locations on the microscope slide. With regard to "processing the plurality of images to identify the proliferative disorder" it is noted that this limitation is an abstract step rather than a active method step, therefore it is not given patentable weight when distinguishing the prior art from the instant invention.

All other rejections and objections as set forth or maintained in the previous Office action are withdrawn in light of applicants amendments.

All claims are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/
Primary Examiner, Art Unit 1643